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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,088	09/12/2003	Andrew Vaillant	16051-9US	6597

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OGILVY RENAULT LLP
1981 MCGILL COLLEGE AVENUE
SUITE 1600
MONTREAL, QC H3A2Y3
CANADA

EXAMINER	
PENG, BO	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,088	VAILLANT ET AL.	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-41* is/are pending in the application.

4a) Of the above claim(s) *39 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to the amendment filed July 31, 2007. Claims 1-38 are cancelled. Claims 39-41 are newly added. Claims 39-41 are pending.

2. New Claims 39 and 41 are directed to an oligonucleotide SEQ ID NO: 24 and an oligonucleotide SEQ ID NO: 22, respectively. Claims 39 and 41 are withdrawn as non-elected because Applicant elected species REP 2006 in a reply filed on March 14, 2006, Accordingly, Claim 40 is under consideration in this office action.

Information Disclosure Statement

3. The information disclosure statement submitted on July 27, 2007 is not considered because Applicant's IDS form 1449 indicates it is for Application 10/661,355, not for the instant application.

Terminal Disclaimer

4. The terminal disclaimer for co-pending applications 10/661, 403, 10/661,402, 10/661,415 and 10/969,812 is approved by the Office.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. The rejection of Claims 3-32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention, **is moot** in view of cancellation of the claims.

Claim Rejections - 35 USC § 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The rejection of Claims 3-32 under 35 U.S.C. 112, first paragraph, is moot in view of cancellation of the claims.

9. Dr. Jean-Marc Juteau's declaration under 37 C.F.R. 1.132 is acknowledged.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. The rejection of Claims 3, 12, 14, 15, 17, 18, 21, 25, 26 and 28-32, under 35 U.S.C. 102(b) as being anticipated by Pan (1995, PANS, 92, pp 11509-11513), **is moot** in view

of cancellation of the claims.

12. The rejection of Claims 3-13 and 16-32 under 35 U.S.C. 102(e), as being anticipated by Davis (US 6,406,705), **is moot** in view of cancellation of the claims.

13. Following are new grounds of rejections necessitated by Applicant's amendment:

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pan (1995, PANS, 92, pp 11509-11513), in view of Davis (US 6,406,705).

16. Claim 40 is directed to an antiviral pharmaceutical composition having anti-HBV activity for treating HBV infection comprising a therapeutically effective amount of REP 2006 and a pharmaceutically acceptable carrier, the anti-HBV activity of said REP 2006 occurs by a non-sequence complementary mode of action. REP is a library of 40-mer oligonucleotides that contains random sequences with phophorothioate linkage.

17. Pan teaches random RNA oligonucleotides having antiviral activity (p.11509-11513). Pan teaches construction of a library of 87-nt oligonucleotides that contain **random 40-nt (40N)** at a central region of the 87-nt oligomer flanked by RSV binding sequences. Pan teaches that DNA library results in double-stranded random DNAs (about $5x10^{15}$ sequences). The random DNAs are then transcribed by T7 RNA polymerase to generate a pool of multiple copies of about 10^{15} RNA sequences (random RNA pool) (Materials and Methods, pp 11509-11510). To increase the RNA stability against the nuclease digestion *in vivo*, Pan teaches that the random RNAs are modified by incorporating 2'-fluro-2-deoxycytidine and 2'-fluro-2-deoxyurine into the RNA chain (2'-F-RNAs). Pan teaches that the random RNAs and 2'-F-RNAs can neutralize RSV particles (Results, pp 11510-11512, and Figures 3 and 4). Pan suggests that such approach can be used to develop RNA and RNA analogs as inhibitors of other viruses (Abstract)

18. Pan does not explicitly teach a 40-mer oligonucleotide that consists of random sequences with phophorothioate linkage.

19. Davis teaches that CpG oligonucleotides (ODN) includes at least the following formula: 5'-$X_1X_2CGX_3X_4$-3' and 5'-$N_1X_1X_2CGX_3X_4N_2$-3'. The CpG ODN may be any size, preferably 8 to 100 nucleotides, **or 8 to 40 nucleotides** in length (Lines 1-32, Column 4, also see Table 1). Davis teaches that chemical modification of the oligonucleotide backbone provides enhanced immunogenicity of the CpG oligonucleotides *in vivo* (Lines 52-62, Column 12). CpG ODN constructs, including at least two phosphorothioate linkages at the 5' end of the oligonucleotide in multiple phosphorothioate linkages at the 3' end, preferably 5, provides maximal activity and protected the oligonucleotide from degradation by intracellular exo- and endo-nucleases.

Davis teaches that such CpG ODN can be used for treating HBV.

20. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Pan's random 87-nt oligonucleotides, which contain **random 40-nt (40N)** at a central region flanked by RSV binding sequences, by deleting RSV binding sequences in order to use the **random 40-nt (40N)** for other viruses, such as HBV, as taught by Davis. The skilled artisan would have been motivated to do so, given the suggestion by Pan and Davis that random oligonucleotides can be used as inhibitors of other viruses. There would have been a reasonable expectation of success, given that the random oligonucleotides can effectively neutralize RSV and HBV as taught by Pan and Davis. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

102/103 Rejection

21. Claim 40 is rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Davis (US 6,406,705).

22. Claim 40 is directed to an antiviral pharmaceutical composition having anti-HBV activity for treating HBV infection comprising a therapeutically effective amount of REP 2006 and a pharmaceutically acceptable carrier, the anti-HBV activity of said REP 2006 occurs by a non-sequence complementary mode of action.

23. Davis teaches that immunostimulatory oligonucleotides having at least one unmethylated CpG dinucleotide (CpG ODN) can be used for induction of cellular immunity against HBV (Abstract, Column 35, Examples 1-6). Davis teaches that CpG ODN includes at least the following formula: 5'-$X_1X_2CGX_3X_4$-3' and 5'-$N_1X_1X_2CGX_3X_4N_2$-3'. The CpG ODN may be

any size, preferably 8 to 100 nucleotides, **or 8 to 40 nucleotides** in length (Lines 1-32, Column 4, also see Table 1). The CpG ODN can be double-stranded or single-stranded (Line 50-55, Column 10 and Column 11). Davis teaches that chemical modification of the oligonucleotide backbone provides enhanced immunogenicity of the CpG oligonucleotides *in vivo* (Lines 52-62, Column 12). CpG ODN constructs, including at least two phosphorothioate linkages at the 5' end of the oligonucleotide in multiple phosphorothioate linkages at the 3' end, preferably 5, provides maximal activity and protected the oligonucleotide from degradation by intracellular exo- and endo-nucleases. Other modified oligonucleotides include phosphodiester-modified oligonucleotides, combinations of phosphodiester and phosphorothioate oligonucleotides, methylphosphonates, methylphosphorothioates, phosphorodithioates, and combinations thereof. Davis teaches that the pharmaceutical compositions of CpG ODN can be administered by intramuscular, intradermal injection, intranasal application, inhalation, topically, intravenously, or orally. CpG ODN can be formulated in liposomes or other drug delivery systems (Line 61, Column 31 to Line 15, Column 32). Davis teaches that the use of CpG ODN as an adjuvant alone or in combination with other adjuvants (Lines 8-13, Column 34).

24. Since REP 2006 is a library of 40-mer oligonucleotides that have random nucleic acid sequences, REP 2006 must contain many 40-mer oligonucleotides that contain CpG. Thus, the claimed REP 2006 must be inherently disclosed by Davis. Where applicant claims a composition in terms of a characteristic not explicitly disclosed by the reference, a 102/103 rejection is proper (MPEP 2112).

25. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the CpG oligonucleotides of the prior art are not the same as the

claimed REP 2006. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed REP 2006 is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Remarks

26. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph. D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

BP

Bo Peng, Ph.D.
October 9, 2007

Bruce Campell

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600